APPENDIX B

Article 34 Amendment
Filed December 15, 2003

ATTORNEY DOCKET NUMBER: 2003946-0018 (ANDI/PCT)

IN THE EUROPEAN PATENT OFFICE
AS INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

Applicant: Eisai Co. Ltd.
Intl. Appln. No.: PCT/US03/07377
Intl. Filing Date: 7 March 2003
Priority: U.S.S.N. 60/362,883 filed 8 March 2002
U.S.S.N. 60/380,711 filed 14 May 2002

For: MACROCYCLIC COMPOUNDS USEFUL AS PHARMACEUTICALS

VIA FACSIMILE
011-49-89-2399-4465
CONFIRMATION BY
INTERNATIONAL COURIER

EUROPEAN PATENT OFFICE
D-80298 MUNICH
GERMANY
Authorized Officer: Examiner

Dear Sir/Madam:

REQUEST FOR AMENDMENT UNDER PCT ARTICLE 34

1. Applicant respectfully requests authorization from the International Preliminary Examining Authority for amendment under PCT Article 34 and respectfully submits that the replacement sheets, as submitted herewith, reflect claim amendments which do not introduce new matter. Applicant submits herewith replacement sheets number 378-379, 379a, 389-390, 390a, 404-405, 405a and 416-418, to replace sheets number 378-379, 389-390, 404-405 and 416-418, originally filed for this application.

2. In respect of each claim appearing in the international application based on replacement sheets 378-379, 379a, 389-390, 390a, 404-405, 405a and 416-418 submitted herewith, and in accordance with PCT Section 205(b), the following claim(s) is/are:

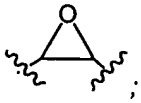
(i) Unchanged: Claims 2, 36, 119-122 and 124 are unchanged;

(ii) Replaced: Claims 1, 37, 84 and 123 are replaced with new claims 1, 37, 84 and 123, respectively;

A marked-up copy of Claim Replacements highlighting the changes is provided herewith as attached Appendix A. Deletions are represented in strikethrough, and additions are represented in underlining.

Applicant respectfully submits that no new matter is presented with these amendments. Specifically, claims 1 and 37, as amended, include the proviso that "*when n is 1; X is O; R_1 is methyl; R_2, R_3, R_7 and R_{11} are each hydrogen; R_5 is hydrogen, C_{1-4}alkyl or –C(=O)C_{1-4}alkyl; R_6 is hydrogen, OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and R_9 is OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; then one or more if the following groups do not occur simultaneously as defined:*

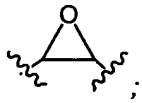
(i) R_4 is hydrogen; R_{10} and R_8 are independently OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is –CH_2CH_2- or –CH=CH-;

(ii) R_4 and R_8 are each hydrogen; R_{10} is OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is –CHR^YCHR^Z-, –CH=CH- or  *; wherein R^Y and R^Z are independently hydrogen, C_{1-4}alkyl or C_{1-4}alkanoyl; and*

(iii) R_4 and R_{10} are each hydrogen, OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; R_8 is hydrogen, OH, halogen, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is –CH_2CH_2-, –CH=CH- or –C(=O)CH_2-." which specifically excludes macrocyclic compounds generically and/or specifically disclosed in references 1-6, and pharmaceutical compositions thereof.

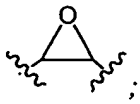
Claim 84, as amended, includes the proviso that "*when n is 1; X is O; R_1 is methyl; R_2, R_3, R_7 and R_{11} are each hydrogen; R_5 is hydrogen, C_{1-4}alkyl or –C(=O)C_{1-4}alkyl; R_6 is hydrogen, OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and R_9 is OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; then one or more if the following groups do not occur simultaneously as defined:*

(i) R_4 is hydrogen; R_{10} and R_8 are independently OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is –CH_2CH_2- or –CH=CH-; and

(ii) R_4 and R_8 are each hydrogen; R_{10} is OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is –CHR^YCHR^Z-, –CH=CH- or  *; wherein R^Y and R^Z are independently hydrogen, C_{1-4}alkyl or C_{1-4}alkanoyl; and*

(iii) R_4 and R_{10} are each hydrogen, OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; R_8 is hydrogen, OH, halogen, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is –CH_2CH_2-, –CH=CH- or –C(=O)CH_2-; whereby the compound induces mRNA degradation and the method is for treating a disorder resulting from cell proliferation", which specifically excludes methods disclosed in references 1, 2 and 3.

Claim 123, as amended, includes the proviso that "*the following groups do not occur simultaneously as defined: n is 1; X is O; R_1 is methyl; R_2, R_3, R_4, R_7, R_8 and R_{11} are each*

hydrogen; R_5 is hydrogen, C_{1-4}alkyl or $-C(=O)C_{1-4}$alkyl; R_6 is hydrogen, OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; R_9 and R_{10} are independently OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and Y-Z is $-CHR^YCHR^Z-$, $-CH=CH-$ or  *; wherein R^Y and R^Z are independently hydrogen, C_{1-4}alkyl or C_{1-4}alkanoyl*", which specifically excludes methods for treating restenosis disclosed in reference 2.

Applicant submits that the amendments to the claims, as described above and detailed herein, do not present new matter. Thus Applicant respectfully requests entry of these amendments, and consideration of these amendments in processing the application.

3. The deletion of any claims and any other loss of claimed subject matter is being made solely to expedite prosecution of the subject matter now claimed, rather than in acquiescence to any positions taken by the Examiner. Applicant is submitting the present amendments without prejudice to the subsequent prosecution of claims to some or all of the subject matter which might be lost by virtue of this paper. Applicant additionally reserves the right to re-introduce the subject matter of any of the canceled claims, or subject matter which might be lost by virtue of amendments set forth in this paper, in the application.

Applicant hereby requests that the ISA begin its examination upon this submission. Favorable action is respectfully requested.

Respectfully submitted,
CHOATE, HALL & STEWART

Dated 15 December 2003

Nadège M. Lagneau, Ph.D.
Agent for Applicant

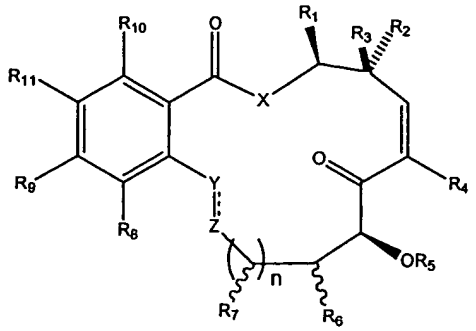
PATENT GROUP
CHOATE, HALL & STEWART
Exchange Place
53 State Street
Boston, MA 02109
Tel: (617) 248-5150
Fax: (617) 248-4000

- APPENDIX A –

VERSION WITH MARKINGS TO SHOW CHANGES MADE

CLAIM REPLACEMENTS

1. A compound having the structure:



(I)

wherein R_1 is hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl;

R_2 and R_3 are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or

R_1 and R_2, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms; or

R_1 and R_3, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms;

R_4 is hydrogen or halogen;

R_5 is hydrogen, an oxygen protecting group or a prodrug;

R_6 is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or an aliphatic moiety optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or a protecting

group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $-(C=O)NHR_{15}$ $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an aliphatic moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

$\mathbf{R_{10}}$ is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

$\mathbf{R_{11}}$ is hydrogen, hydroxyl or protected hydroxyl;

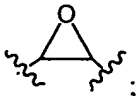
X is absent or is O, NH, N-alkyl, CH_2 or S;

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and **Z** is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or aliphatic, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or lower alkyl, and Y and Z may be connected by a single or double bond; and

pharmaceutically acceptable derivatives ~~thereof.~~ thereof;

with the proviso that when n is 1; X is O; R_1 is methyl; R_2, R_3, R_7 and R_{11} are each hydrogen; R_5 is hydrogen, C_{1-4}alkyl or $-C(=O)C_{1-4}$alkyl; R_6 is hydrogen, OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and R_9 is OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; then one or more if the following groups do not occur simultaneously as defined:

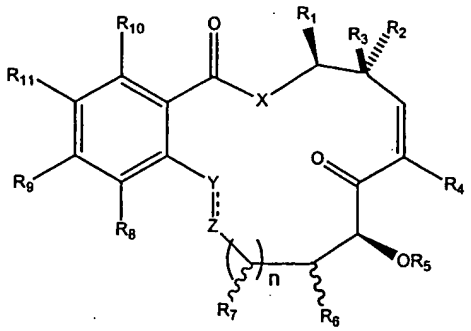
(i) R_4 is hydrogen; R_{10} and R_8 are independently OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and Y-Z is $-CH_2CH_2-$ or $-CH=CH-$;

(ii) R_4 and R_8 are each hydrogen; R_{10} is OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and Y-Z is $-CHR^YCHR^Z-$, $-CH=CH-$ or  ; wherein R^Y and R^Z are independently hydrogen, C_{1-4}alkyl or C_{1-4}alkanoyl; and

(iii) R_4 and R_{10} are each hydrogen, OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; R_8 is hydrogen, OH, halogen, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and Y-Z is $-CH_2CH_2-$, $-CH=CH-$ or $-C(=O)CH_2-$.

37. A pharmaceutical composition comprising:

a compound having the structure:



(I)

wherein $\mathbf{R_1}$ is hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl;

$\mathbf{R_2}$ and $\mathbf{R_3}$ are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or

R_1 and R_2, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms; or

R_1 and R_3, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms;

$\mathbf{R_4}$ is hydrogen or halogen;

$\mathbf{R_5}$ is hydrogen, an oxygen protecting group or a prodrug;

$\mathbf{R_6}$ is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or an aliphatic moiety optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $-(C=O)NHR_{15}$ $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an aliphatic moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R_{11} is hydrogen, hydroxyl or protected hydroxyl;

X is absent or is O, NH, N-alkyl, CH_2 or S;

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and Z is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or aliphatic, or R_{17} and R_{18} taken

together is –O-, -CH_2- or -NR_{19}-, wherein R_{19} is hydrogen or lower alkyl, and Y and Z may be connected by a single or double bond; pharmaceutically acceptable derivatives thereof; and

a pharmaceutically acceptable ~~carrier.~~ carrier;

with the proviso that when n is 1; X is O; R_1 is methyl; R_2, R_3, R_7 and R_{11} are each hydrogen; R_5 is hydrogen, C_{1-4}alkyl or –C(=O)C_{1-4}alkyl; R_6 is hydrogen, OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and R_9 is OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; then one or more if the following groups do not occur simultaneously as defined:

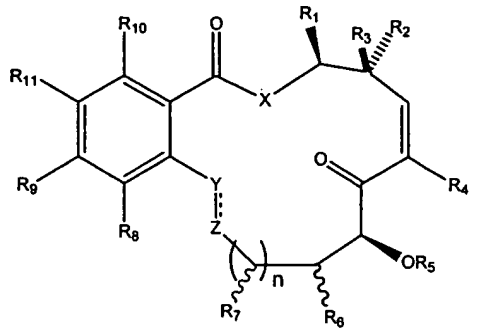
(i) R_4 is hydrogen; R_{10} and R_8 are independently OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is –CH_2CH_2- or –CH=CH-;

(ii) R_4 and R_8 are each hydrogen; R_{10} is OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is –CHR^YCHR^Z-, –CH=CH- or  ; wherein R^Y and R^Z are independently hydrogen, C_{1-4}alkyl or C_{1-4}alkanoyl; and

(iii) R_4 and R_{10} are each hydrogen, OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; R_8 is hydrogen, OH, halogen, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is –CH_2CH_2-, –CH=CH- or –C(=O)CH_2-.

84. A method for treating an inflammatory and/or autoimmune disorder or a disorder resulting from increased angiogenesis and/or cell proliferation comprising:

administering to a subject in need thereof a therapeutically effective amount of a compound having the structure:



(I)

wherein $\mathbf{R_1}$ is hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl;

$\mathbf{R_2}$ and $\mathbf{R_3}$ are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or

R_1 and R_2, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms; or

R_1 and R_3, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms;

$\mathbf{R_4}$ is hydrogen or halogen;

$\mathbf{R_5}$ is hydrogen, an oxygen protecting group or a prodrug;

$\mathbf{R_6}$ is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

$\mathbf{R_7}$, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

$\mathbf{R_8}$ is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or an aliphatic moiety optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

$\mathbf{R_9}$ is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $-(C=O)NHR_{15}$ $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an aliphatic moiety, wherein one or

more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R_{11} is hydrogen, hydroxyl or protected hydroxyl;

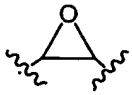
X is absent or is O, NH, N-alkyl, CH_2 or S;

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and **Z** is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or aliphatic, or R_{17} and R_{18} taken together is –O-, -CH_2- or -NR_{19}-, wherein R_{19} is hydrogen or lower alkyl, and Y and Z may be connected by a single or double bond; pharmaceutically acceptable derivatives thereof; and

a pharmaceutically acceptable carrier or ~~diluent.~~ diluent;

with the proviso that when n is 1; X is O; R_1 is methyl; R_2, R_3, R_7 and R_{11} are each hydrogen; R_5 is hydrogen, C_{1-4}alkyl or –C(=O)C_{1-4}alkyl; R_6 is hydrogen, OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and R_9 is OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; then one or more if the following groups do not occur simultaneously as defined:

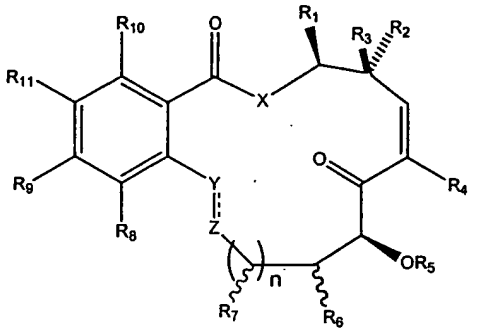
(i) R_4 is hydrogen; R_{10} and R_8 are independently OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is –CH_2CH_2- or –CH=CH-; and

(ii) R_4 and R_8 are each hydrogen; R_{10} is OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is –CHR^YCHR^Z-, –CH=CH- or  ; wherein R^Y and R^Z are independently hydrogen, C_{1-4}alkyl or C_{1-4}alkanoyl; and

(iii) R_4 and R_{10} are each hydrogen, OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; R_8 is hydrogen, OH, halogen, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is –CH_2CH_2-, –CH=CH- or –C(=O)CH_2-; whereby the compound induces mRNA degradation and the method is for treating a disorder resulting from cell proliferation.

123. A method for preventing or reducing the rate of restenosis, comprising:

inserting a stent into an obstructed blood vessel, the stent having a generally tubular structure, the surface of the structure being coated with (or otherwise adapted to release) a composition comprising a compound having the structure:



(I)

wherein R_1 is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R_2 and R_3 are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, straight or branched lower alkyl, straight or branched lower heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

R_1 and R_2, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen; or

R_1 and R_3, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R_4 is hydrogen or halogen;

R_5 is hydrogen or a protecting group;

R_6 is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or lower alkyl optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, -$X_1(CH_2)_pX_2$-R_{14}, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or -$X_1(CH_2)_pX_2$-R_{14};

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, lower alkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is – (C=O)NHR_{15} –(C=O)OR_{15}, or –(C=O)R_{15}, wherein each occurrence of R_{15} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or R_{14} is –$SO_2(R_{16})$, wherein R_{16} is an alkyl moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R_{11} is hydrogen, hydroxyl or protected hydroxyl;

X is absent or is O, NH, N-alkyl, CH_2 or S;

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and Z is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or lower alkyl, or R_{17} and R_{18} taken together is –O-, -CH_2- or -NR_{19}-, wherein R_{19} is hydrogen or lower alkyl, and Y and Z may be connected by a single or double bond; pharmaceutically acceptable derivatives thereof; and optionally

a pharmaceutically acceptable carrier or diluent;

such that the obstruction is eliminated and the composition is delivered in amounts effective to prevent or reduce the rate of ~~restenosis.~~ restenosis;

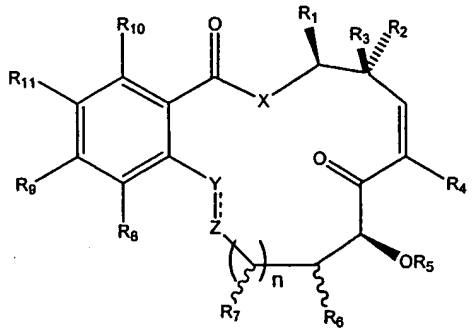
with the proviso that the following groups do not occur simultaneously as defined: n is 1; X is O; R_1 is methyl; R_2, R_3, R_4, R_7, R_8 and R_{11} are each hydrogen; R_5 is hydrogen, C_{1-4}alkyl or $-C(=O)C_{1-4}$alkyl; R_6 is hydrogen, OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; R_9 and R_{10} are independently OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and Y-Z is $-CHR^YCHR^Z-$, -CH=CH- or  ; wherein R^Y and R^Z are independently hydrogen, C_{1-4}alkyl or C_{1-4}alkanoyl.

SUBSTITUTE SHEETS

CLAIMS

We claim:

1. A compound having the structure:



(I)

wherein R_1 is hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl;

R_2 and R_3 are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or

R_1 and R_2, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms; or

R_1 and R_3, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms;

R_4 is hydrogen or halogen;

R_5 is hydrogen, an oxygen protecting group or a prodrug;

R_6 is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or an aliphatic moiety optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $-(C=O)NHR_{15}$ $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an aliphatic moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

$\mathbf{R_{10}}$ is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

$\mathbf{R_{11}}$ is hydrogen, hydroxyl or protected hydroxyl;

X is absent or is O, NH, N-alkyl, CH_2 or S;

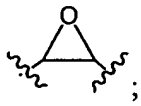
Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and **Z** is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or aliphatic, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or lower alkyl, and Y and Z may be connected by a single or double bond; and

pharmaceutically acceptable derivatives thereof;

with the proviso that when n is 1; X is O; R_1 is methyl; R_2, R_3, R_7 and R_{11} are each hydrogen; R_5 is hydrogen, C_{1-4}alkyl or $-C(=O)C_{1-4}$alkyl; R_6 is hydrogen, OH, C_1-

$_4$alkoxy or –OC(=O)C_{1-4}alkyl; and R_9 is OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; then one or more if the following groups do not occur simultaneously as defined:

(i) R_4 is hydrogen; R_{10} and R_8 are independently OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is $–CH_2CH_2-$ or –CH=CH-;

(ii) R_4 and R_8 are each hydrogen; R_{10} is OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is $–CHR^YCHR^Z-$, –CH=CH- or  ; wherein R^Y and R^Z are independently hydrogen, C_{1-4}alkyl or C_{1-4}alkanoyl; and

(iii) R_4 and R_{10} are each hydrogen, OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; R_8 is hydrogen, OH, halogen, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is $–CH_2CH_2-$, –CH=CH- or $–C(=O)CH_2-$.

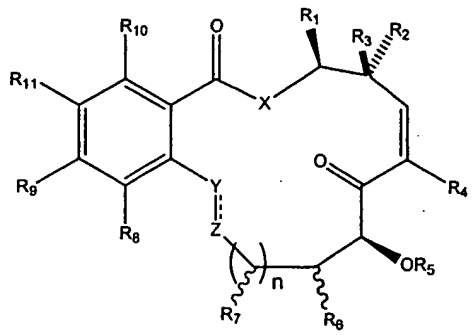
2. The compound of claim 1, where the following groups do not occur simultaneously as defined:

X is oxygen,

and pharmaceutically acceptable derivatives thereof.

37. A pharmaceutical composition comprising:

a compound having the structure:



(I)

wherein $\mathbf{R_1}$ is hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl;

$\mathbf{R_2}$ and $\mathbf{R_3}$ are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or

R_1 and R_2, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms; or

R_1 and R_3, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms;

$\mathbf{R_4}$ is hydrogen or halogen;

$\mathbf{R_5}$ is hydrogen, an oxygen protecting group or a prodrug;

$\mathbf{R_6}$ is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

$\mathbf{R_7}$, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

$\mathbf{R_8}$ is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or an aliphatic moiety optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

$\mathbf{R_9}$ is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is – $(C=O)NHR_{15}$ –$(C=O)OR_{15}$, or –$(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or R_{14} is $–SO_2(R_{16})$, wherein R_{16} is an aliphatic moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

$\mathbf{R_{10}}$ is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

$\mathbf{R_{11}}$ is hydrogen, hydroxyl or protected hydroxyl;

X is absent or is O, NH, N-alkyl, CH_2 or S;

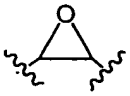
Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and **Z** is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or aliphatic, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or lower alkyl, and Y and Z may be connected by a single or double bond; pharmaceutically acceptable derivatives thereof; and

a pharmaceutically acceptable carrier;

with the proviso that when n is 1; X is O; R_1 is methyl; R_2, R_3, R_7 and R_{11} are each hydrogen; R_5 is hydrogen, C_{1-4}alkyl or $–C(=O)C_{1-4}$alkyl; R_6 is hydrogen, OH, C_1-

$_4$alkoxy or –OC(=O)C_{1-4}alkyl; and R_9 is OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; then one or more if the following groups do not occur simultaneously as defined:

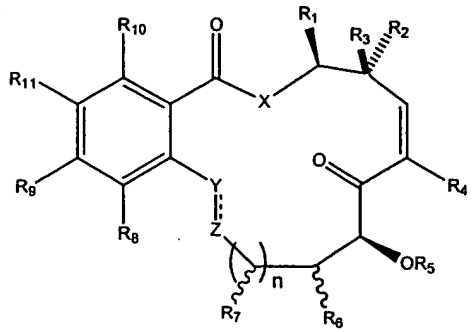
(i) R_4 is hydrogen; R_{10} and R_8 are independently OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is $–CH_2CH_2-$ or –CH=CH-;

(ii) R_4 and R_8 are each hydrogen; R_{10} is OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is $–CHR^YCHR^Z-$, –CH=CH- or  ; wherein R^Y and R^Z are independently hydrogen, C_{1-4}alkyl or C_{1-4}alkanoyl; and

(iii) R_4 and R_{10} are each hydrogen, OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; R_8 is hydrogen, OH, halogen, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is $–CH_2CH_2-$, –CH=CH- or $–C(=O)CH_2-$.

84. A method for treating an inflammatory and/or autoimmune disorder or a disorder resulting from increased angiogenesis and/or cell proliferation comprising:

administering to a subject in need thereof a therapeutically effective amount of a compound having the structure:



(I)

wherein $\mathbf{R_1}$ is hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl;

$\mathbf{R_2}$ and $\mathbf{R_3}$ are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or

R_1 and R_2, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms; or

R_1 and R_3, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms;

$\mathbf{R_4}$ is hydrogen or halogen;

$\mathbf{R_5}$ is hydrogen, an oxygen protecting group or a prodrug;

$\mathbf{R_6}$ is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

$\mathbf{R_7}$, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

$\mathbf{R_8}$ is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or an aliphatic moiety optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

$\mathbf{R_9}$ is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is – (C=O)NHR_{15} –(C=O)OR_{15}, or –(C=O)R_{15}, wherein each occurrence of R_{15} is independently hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or R_{14} is $–SO_2(R_{16})$, wherein R_{16} is an aliphatic moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R_{11} is hydrogen, hydroxyl or protected hydroxyl;

X is absent or is O, NH, N-alkyl, CH_2 or S;

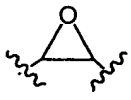
Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and **Z** is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or aliphatic, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or lower alkyl, and Y and Z may be connected by a single or double bond; pharmaceutically acceptable derivatives thereof; and

a pharmaceutically acceptable carrier or diluent;

with the proviso that when n is 1; X is O; R_1 is methyl; R_2, R_3, R_7 and R_{11} are each hydrogen; R_5 is hydrogen, C_{1-4}alkyl or $–C(=O)C_{1-4}$alkyl; R_6 is hydrogen, OH, C_1-

$_4$alkoxy or –OC(=O)C_{1-4}alkyl; and R_9 is OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; then one or more if the following groups do not occur simultaneously as defined:

(i) R_4 is hydrogen; R_{10} and R_8 are independently OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is $–CH_2CH_2-$ or –CH=CH-; and

(ii) R_4 and R_8 are each hydrogen; R_{10} is OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is $–CHR^YCHR^Z-$, –CH=CH- or  ; wherein R^Y and R^Z are independently hydrogen, C_{1-4}alkyl or C_{1-4}alkanoyl; and

(iii) R_4 and R_{10} are each hydrogen, OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; R_8 is hydrogen, OH, halogen, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is $–CH_2CH_2-$, –CH=CH- or $–C(=O)CH_2-$; whereby the compound induces mRNA degradation and the method is for treating a disorder resulting from cell proliferation.

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and Z is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or lower alkyl, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or lower alkyl, and Y and Z may be connected by a single or double bond; pharmaceutically acceptable derivatives thereof; and

a pharmaceutically acceptable carrier or diluent.

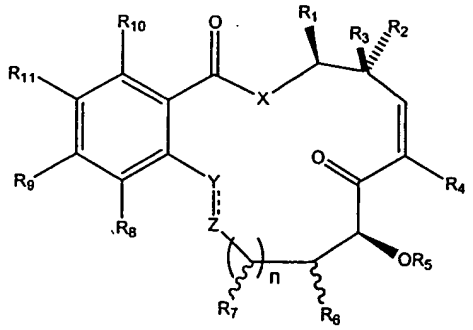
120. The method of claim 119, wherein in the step of administering, the composition is administerd topically.

121. The method of claim 119, wherein the photodamage is skin wrinkles.

122. The method of claim 119, wherein the photodamage is a skin cancer.

123. A method for preventing or reducing the rate of restenosis, comprising:

inserting a stent into an obstructed blood vessel, the stent having a generally tubular structure, the surface of the structure being coated with (or otherwise adapted to release) a composition comprising a compound having the structure:



(I)

wherein $\mathbf{R_1}$ is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

$\mathbf{R_2}$ and $\mathbf{R_3}$ are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, straight or branched lower alkyl, straight or branched lower heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

R_1 and R_2, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen; or

R_1 and R_3, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

$\mathbf{R_4}$ is hydrogen or halogen;

$\mathbf{R_5}$ is hydrogen or a protecting group;

$\mathbf{R_6}$ is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

$\mathbf{R_7}$, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

$\mathbf{R_8}$ is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or lower alkyl optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

$\mathbf{R_9}$ is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, lower alkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $-(C=O)NHR_{15}$ $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each

occurrence of R_{15} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an alkyl moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

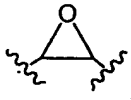
R_{11} is hydrogen, hydroxyl or protected hydroxyl;

X is absent or is O, NH, N-alkyl, CH_2 or S;

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and **Z** is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or lower alkyl, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or lower alkyl, and Y and Z may be connected by a single or double bond; pharmaceutically acceptable derivatives thereof; and optionally

a pharmaceutically acceptable carrier or diluent;

such that the obstruction is eliminated and the composition is delivered in amounts effective to prevent or reduce the rate of restenosis;

with the proviso that the following groups do not occur simultaneously as defined: n is 1; X is O; R_1 is methyl; R_2, R_3, R_4, R_7, R_8 and R_{11} are each hydrogen; R_5 is hydrogen, C_{1-4}alkyl or $-C(=O)C_{1-4}$alkyl; R_6 is hydrogen, OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; R_9 and R_{10} are independently OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and Y-Z is $-CHR^YCHR^Z-$, –CH=CH- or  ; wherein R^Y and R^Z are independently hydrogen, C_{1-4}alkyl or C_{1-4}alkanoyl.

124. A method for expanding the lumen of a body passageway, comprising:

inserting a stent into the passageway, the stent having a generally tubular structure, the surface of the structure being coated with (or otherwise adapted to release) a composition comprising a compound having the structure: